

## REMARKS/ARGUMENTS

### Status of the Claims

In order to further prosecution, and not for reasons related to patentability, independent claims 5, 13, 19, and 42 have been amended to include the limitation that the compositions are prepared using a method “consisting essentially of” the recited steps. Support for limiting the method of preparation to the recited steps resides throughout the specification, for example, in the Experimental section. No new matter is added by way of claim amendment. Applicants expressly reserve the right to pursue continuation applications or take other such appropriate measures to seek protection of the broader subject matter recited in the original claims.

Claims 5-9, 13-17, and 19-49 are pending in the application. Reexamination and reconsideration of the claims is respectfully requested in view of these amendments and the following remarks. The Examiner’s comments in the Office Action are addressed below in the order set forth therein.

### The Rejections of the Claims Under 35 U.S.C. §103(a) Should Be Withdrawn

Claims 5-9, 13-17, 19-44, and 46-49 are newly rejected under 35 U.S.C. §103(a) as being unpatentable over Dorin *et al.*, U.S. Patent 5,814,485 (hereinafter the “Dorin *et al.* patent”) in view of Hershenson *et al.*, U.S. Patent 5,004,605 (hereinafter the “Hershenson *et al.* patent”). Claims 5-9, 13-17, and 19-49 are rejected under this same statute as being unpatentable over these two cited references, further in view of *The Merck Index* (1989). These rejections are both respectfully traversed.

Amended independent claims 5, 13, 19, and 42 set forth the limitation that the IFN- $\beta$  compositions having a pH of about 3.0 to about 5.0 are prepared using a method consisting essentially of the recited steps. All other claims directly or indirectly depend from these independent claims. Accordingly, the claimed IFN- $\beta$  compositions do not comprise glycerol or polyethylene glycol polymers as stabilizing agents.

As previously noted, the Dorin *et al.* patent teaches methods of recombinant production of IFN- $\beta$  and its subsequent purification, and discloses various excipients that can be included in IFN- $\beta$  formulations having a pH of about 6.0 to 7.5. Thus, the Dorin *et al.* compositions have a

pH that is outside the range of the pH of the presently claimed IFN- $\beta$  compositions. Though glycine is taught as an “amorphous protectant” that can be added to these compositions, it is not taught in the context of a buffering agent (for suitable buffers, see the specification at col. 13, lines 44-54).

The Office Action relies on the Hershenson *et al.* patent to provide the guidance that IFN- $\beta$  compositions can be formulated at a low pH overlapping the presently claimed pH range. Applicants respectfully submit that the combined teachings of these two patents do not render the presently claimed compositions obvious.

The Hershenson *et al.* patent teaches “a therapeutically effective amount of a recombinant interferon- $\beta$  protein dissolved in an inert carrier medium comprising as a stabilizer/solubilizer an effective amount either of glycerol or of polyethylene glycol polymers having an average molecular weight from about 190 to about 1600 daltons.” See, for example, column 4, lines 42-48 of the Hershenson *et al.* patent. Hershenson *et al.* explain that “[t]he pharmaceutical compositions of this invention provide a means of maintaining recombinant IFN- $\beta$  in soluble form and thereby stabilizing it by use of one or more solubilizer/stabilizers of this invention.” Column 6, lines 65-68. The Hershenson *et al.* patent thus teaches compositions that require the use of one or more solubilizers/stabilizers to maintain a solubilized interferon formulation.

In contrast, Applicants’ method of formulating IFN- $\beta$  yields compositions that are free of glycerol and polyethylene glycol polymers. The Hershenson *et al.* patent provides no guidance whatsoever, alone or in combination with the Dorin *et al.* patent, that would lead one of skill in the art to formulate IFN- $\beta$  in the manner set forth in the presently claimed invention. Rather, it teaches away from Applicants’ claimed invention.

*The Merck Index* is cited as teaching aspartic acid as a weak acid with a pKa that would be recognized by one of skill in the art as being useful in the presently claimed pH range. However, even if the teachings of *The Merck Index* are combined with the teachings of the Dorin *et al.* and Hershenson *et al.* patents, the combined teachings still fail to provide the guidance to formulate IFN- $\beta$  in the absence of the solubilizer/stabilizers taught as critical components of the Hershenson *et al.* compositions.

Appl. No.: 10/035,420  
Amdt. Dated April 8, 2005  
Reply to Office Action of November 8, 2004

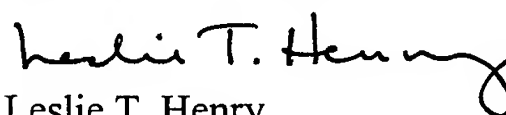
In view of these remarks, Applicants respectfully submit that these three cited references, alone or in combination, fail to teach or suggest the presently claimed compositions. Accordingly, these rejections of the claims should be withdrawn.

### CONCLUSION

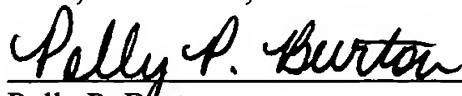
In view of the aforementioned amendments and remarks, Applicants respectfully submit that the rejections of the claims under 35 U.S.C. §103 are overcome and that the claims are patentable over the art cited by the Examiner. Accordingly, Applicants submit that this application is now in condition for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



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